penicillanic acid S,S-dioxide (IVa) could be smoothly converted to sulbactam I (80–90% yield) by a catalytic hydrogenation (5% Pd/C). A two-phase (ethyl acetate/aqueous sodium bicarbonate) system was employed to minimize the exposure of product to hydrogen bromide. With this procedure sulbactam I is produced in ca.. 54–65% overall yield from 6-APA (II).

Experimental Section

Melting points were determined with a Thomas-Hoover capillary apparatus and are uncorrected. Infrared spectra were recorded by using Perkin-Elmer Model 21 and Model 727B spectrometers. NMR spectra were obtained with a Varian XL-100 spectrometer with Me_4Si as an internal standard. Mass spectra were taken with an AEI MS-30 mass spectrometer. Microanalyses were performed by the Pfizer Analytical Department.

6,6-Dibromopenicillanic Acid (IIIa). To a 2-L three-necked, round-bottomed flask equipped with a paddle stirrer and thermometer and containing methylene chloride (500 mL) cooled to about 5 °C were added bromine (119.9 g, 38.5 mL, 0.75 mol), 2.5 N sulfuric acid (200 mL), and sodium nitrite (34.5 g, 0.50 mol). Some foaming was observed upon addition of the sodium nitrite, but there was no exotherm. 6-APA (54.0 g, 0.25 mol) was added portionwise over a period of 30 min. The pot temperature was maintained at 4–10 °C. The resultant dark red solution was stirred at 5 °C for 30 min. A solution of 1 M sodium bisulfite (410 mL) was added dropwise at 5–15 °C over a period of 20 min until the bromine color was discharged, forming a light yellow solution. The organic layer was separated and the aqueous layer extracted with methylene chloride (2 × 150 mL). The combined organic extract was washed with brine (2 × 200 mL) and used in the second step of the process.

The organic extract can be concentrated to afford, in 80% yield, 6,6-dibromopenicillanic acid (IIIa): mp 144–146 °C; IR (KBr) ν_{max} 2600–3700, 1799, 1775 cm^{-1}; NMR ($CDCl_3/Me_2SO$) δ 1.60 (3 H, s, CH_3), 1.70 (3 H, s, CH_3), 4.57 (1 H, s, 3-H), 5.92 (1 H, s, 5-H). IIIa is more stable as its sodium salt: mp 205 °C; $[\alpha]^{20}_D$ +210° (c 0.01, pH 5 buffer); IR (KBr) ν_{max} 2600–3700, 1779, 1712 cm^{-1}; NMR ($CDCl_3/D_2O$) δ 1.47 (3 H, s, CH_3), 1.58 (3 H, s, CH_3), 4.35 (1 H, s, 3-H), 5.83 (1 H, s, 5-H). Anal. Calcd for $C_8H_8NO_3Br_2Na$: C, 25.22; H, 2.12; N, 3.68; S, 8.42. Found: C, 24.97; H, 2.48; N, 3.65; S, 8.24.

In a similar fashion, IIId [mp 148–152 °C; 58% yield; IR (KBr) ν_{max} 2500–3570, 1779, 1712 cm^{-1}; NMR ($CDCl_3/Me_2SO$) δ 1.50 (3 H, s, CH_3), 1.67 (3 H, s, CH_3), 4.50 (1 H, s, 3-H), 5.43 (1 H, s, 5-H)] and IIIe [mp 145–147 °C; 72% yield; IR (KBr) ν_{max} 2500–3571, 1786, 1718 cm^{-1}; NMR ($CDCl_3/Me_2SO$) 1.53 (3 H, s, CH_3), 1.67 (3 H, s, CH_3), 4.46 (1 H, s, 3-H), 5.57 (1 H, s, 5-H)] were prepared.

6,6-Dibromopenicillanic Acid S,S-Dioxide (IVa). To a 4-L beaker equipped with a mechanical stirrer and containing the methylene chloride solution from step I (~800 mL) was added water (300 mL) followed by the dropwise addition over a period of 30 min of 3 N sodium hydroxide (105 mL) until the pH stabilized at 7.0. The aqueous layer was separated, and the organic layer was again extracted with water (1 × 200 mL). To the combined aqueous layers which were placed in a 2-L, three-necked, round-bottomed flask equipped with a mechanical stirrer and cooled to −5 °C was added a premixed solution containing potassium permanganate (59.25 g, 0.38 mol), 85% phosphoric acid (18 mL, 0.31 mol), and water (600 mL) over a period of 50 min until the oxidation was complete as indicated by the persistence of the dark purple permanganate color (550 mL). The pH of this solution stabilized at 6.2. Following the addition, ethyl acetate (500 mL) was added, and the pH of the purple solution was lowered to 1.23 with 6 N hydrochloric acid (150 mL). To this biphasic solution was added dropwise a 1 M sodium bisulfite solution (250 mL) over a period of 10–15 min as the temperature was kept below 10 °C, and the pH was maintained at 1.25–1.35 by using 6 N hydrochloric acid (60 mL). The aqueous layer was then saturated with sodium chloride, and the two phases were separated. The aqueous solution was reextracted with additional ethyl acetate (2 × 150 mL), and the combined organic extracts were washed with brine (2 × 200 mL), dried over magnesium sulfate, filtered, and carried into the hydrogenation step. The desired product, 6,6-dibromopenicillanic acid S,S-dioxide (IVa, mp 201 °C dec) can be isolated at this stage (~72% yield from 6-APA): $[\alpha]^{20}_D$ +204.5° (c 0.01, pH 5 buffer); IR (KBr) ν_{max} 2700–3250, 1812, 1743, 1462, 1337 cm^{-1}; NMR ($CDCl_3/Me_2SO$), 1.49 (3 H, s, CH_3), 1.63 (3 H, s, CH_3), 4.49 (1 H, s, 3-H), 5.41 (1 H, s, 5-H). Anal. Calcd for $C_8H_9NO_5Br_2S$: C, 24.57; H, 2.32; N, 3.58; Br, 40.87. Found: C, 24.70; H, 2.39; N, 3.61; Br, 40.66.

Sulbactam (I). In a 2-L Parr bottle were combined the ethyl acetate extract from step 2 containing 6,6-dibromopenicillanic acid S,S-dioxide (IVa, 705 mL), a saturated sodium bicarbonate solution (705 mL), and 5% Pd/C catalyst (50% water wet, 8.88 g). Some foaming occurred. The mixture was placed on a Parr shaker, purged with nitrogen, and hydrogenated under ~50 psi pressure for 1.25 h. The mixture was then purged with nitrogen and filtered through a Celite pad. After the filtrate was cooled to ~5 °C, the pH was adjusted to 1.2 with 6 N hydrochloric acid (77 mL). The aqueous layer was saturated with brine, the layers were separated, and the resultant aqueous layer was reextracted with ethyl acetate (3 × 200 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated in vacuo to afford 33.5 g (57.5%) of crude product as a light yellow solid. Sulbactam was obtained in pure form by dissolving the crude product in ethyl acetate (600 mL), heating (~35 °) the solution with Darco, filtering, and concentrating this solution in vacuo to yield a white solid which was slurried in hexane (200 mL) and filtered to give 31.0 g (54%) of sulbactam: mp 170 °C dec; $[\alpha]^{20}_D$ +251° (c = 0.01, pH 5.0 buffer); IR (KBr) ν_{max} 2500–3636, 1786, 1754 cm^{-1}; NMR (Me_2SO) 1.37 (3 H, s, CH_3), 1.48 (3 H, s, CH_3), 3.23 (1 H, dd, J = 1.7, 16.4 Hz, 6β-H), 3.64 (1 H, dd, J = 4.4, 16.4 Hz, 6α-H), 4.26 (1 H, s, 3-H), 5.13 (1 H, dd, J = 1.7, 4.4 Hz, 5-H). Anal. Calcd for $C_8H_{11}NO_5S$: C, 41.20; H, 4.76; N, 6.00; S, 13.75. Found: C, 41.43; H, 4.72; N, 6.05; S, 13.76.

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Registry No. I, 68373-14-8; II, 551-16-6; IIIa, 24158-88-1; IIId, 76517-06-1; IIIe, 76517-24-3; IVa, 76646-91-8; IIIa Na, 76454-48-3.

Nitration of 2-Alkoxytoluenes: Formation of Biphenyl Derivatives

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In the nitration of aromatic compounds, a number of side reactions have been uncovered, thereby leading to an increase in the utility of this reaction for functionalization.[1] We here report on a coupling reaction which occurs when 2-alkoxytoluenes are nitrated. Although nitration of 2-alkoxytoluenes has been reported, the formation of biphenyl derivatives has not been claimed previously. Thus, Staedel[2] reported the preparation of mononitro- and dinitro-2-ethoxytoluenes by nitration of 2-ethoxytoluene in concentrated nitric acid. Nitration of 2-methylanisole in aqueous nitric–sulfuric acid afforded a mixture of 4- and 6-nitro-2-methylanisole as well as the corresponding phenolic byproducts.[3]

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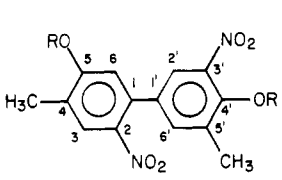
0022-3263/82/1947-3345$01.25/0

Table I. ^{13}C NMR Data for the Aromatic Region of Biphenyl Derivatives[a]



I II

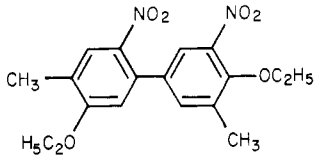
R for I	chemical shift, δ											
	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)	C(6′)
CH_3	134.6	143.9	128.0	122.4	161.0	112.5	134.6	128.0	140.6	151.4	127.4	135.1
C_2H_5	134.7	144.2	134.5	122.4	160.5	113.3	134.7	128.0	140.5	150.6	127.5	135.0
C_3H_7	134.7	144.1	134.5	122.4	160.7	113.3	134.7	131.0	140.4	150.6	127.9	135.1

[a] For II the chemical shifts in δ units are given on the structure.

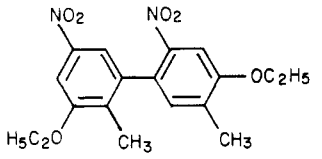
Results and Discussion

Addition of 2-ethoxytoluene to a 70% aqueous nitric acid solution at −10 to −5 °C produced a rapid color change of the reaction mixture. Workup of the resulting mixture (see Experimental Section) gave a mixture containing two major and several minor products as indicated by TLC. Separation of this mixture by preparatory high-performance liquid chromatography afforded a mononitroethoxytoluene derivative and a dinitro product which the mass spectrum indicated to be a biphenyl derivative. In addition, a more polar mixture, constituting about 7% of the total weight, was obtained which could not be separated under the conditions employed.

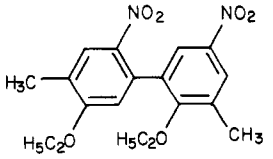
The aromatic region of the ^1H NMR spectrum ($CDCl_3$) of the mononitro derivative, 2-ethoxy-5-nitrotoluene, consisted of signals at δ 8.08 (1 H, dd, J_o = 9 Hz, J_m = 2 Hz), 8.0 (1 H, d, J_m = 2 Hz), and 6.79 (1 H, d, J_o = 9 Hz). Two pairs of proton signals were present in the corresponding region of the ^1H NMR spectrum of the biphenyl product. One pair, due to the presence of a meta-related pair of protons, occurred as doublets (J_m = 2.5 Hz) at δ 7.54 and 7.21, and a second pair, indicative of a para-related pair of protons, appeared as a broad singlets at δ 7.82 and 6.59. On the basis of these data and mechanistic considerations, three probable structures (**1**, **2**, and **3**) were envisaged for the biphenyl compound.



1



2



3

Comparison of calculated ^{13}C NMR data for structures **1**–**3** with the experimental values (Table I) suggested that **1** correctly represented the product. The results of a single-crystal X-ray analysis confirmed this structure assignment and provided details of the solid-state geometry.

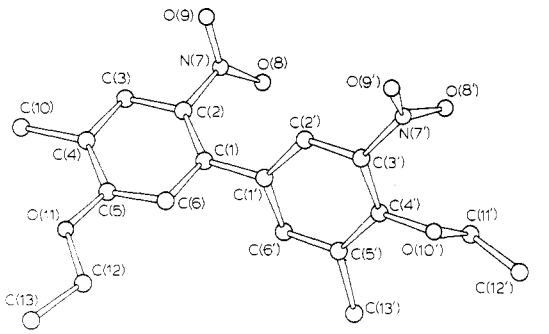


Figure 1. Atom-numbering scheme and solid-state conformation of **1**.

The crystal structure of **1** was solved by direct methods.[4] Least-squares refinement of atomic positional and thermal parameters converged to R = 0.076[5] over 923 reflections measured by a diffractometer. A view of the structure is provided in Figure 1. Final nonhydrogen atom positional parameters are in Table II;[6] bond lengths are presented in Figure 2.[6] Displacements of selected atoms from least-squares planes through groups of atoms and torsion angles defining the molecular conformation are in Tables III and IV,[6] repectively.

Bond lengths and endocyclic angles lie close to corresponding values in other nitrobenzene and biphenyl derivatives.[7] Relief from severe steric overcrowding involving adjacent phenyl ring substituents is gained by various combinations of significant exocyclic bond angle deformation with out-of-plane twisting and bending. Thus, the dihedral angles between the plane through C(1)–C(6) and those through C(2), N(7), O(8), O(9), and C(1′)–C(6′) are 34.8 and 46.7°, respectively. In addition, the highly significant enlargements of the C(1)–C(2)–N(7) and C(2)–C(1)–C(1′) angles over the smaller C(3)–C(2)–N(7) and C(6)–C(1)–C(1′) angles serve to alleviate nonbonded interactions between the *C(2)*-nitro and *C(1)*-phenyl ring B substituents. At C(5), the ethoxy substituent adopts the usual preferred conformation, with C(12) lying close to the phenyl ring plane.[8] Repulsive nonbonded interactions

(3) J. W. Barnett, R. B. Moodie, K. Schofield, J. B. Weston, R. G. Coombes, J. G. Golding, and G. D. Tobin, *J. Chem. Soc., Perkin Trans. 2*, 248 (1977).

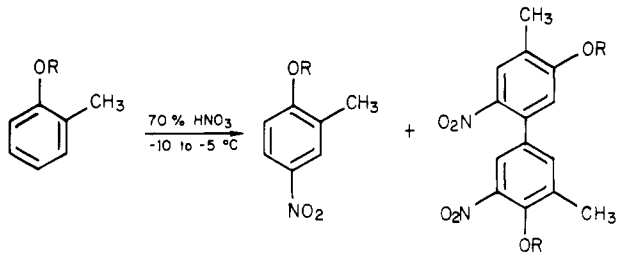
(4) P. Main, L. Lessinger, M. M. Woolfson, G. Germain, and J.-P. Declerq, "MULTAN76, A System of Computer Programs for the Automatic Solution of Crystal Structures", Universities of York, England, and Louvain, Belgium, 1976.

(5) $R = \sum||F_o| - |F_c||/\sum|F_o|$.

(6) Supplementary material; see the paragraph at the end of the paper.

(7) O. L. Carter, A. T. McPhail, and G. A. Sim, *J. Chem. Soc. A*, 822 (1966); G.-P. Charbonneau and Y. Delugeard, *Acta Crystallogr., Sect. B*, **B32**, 1420 (1976); L. Fallon, III, and H. L. Ammon, *J. Cryst. Mol Struct.*, 4, 63 (1974); G. Casalone, A. Gavezzotti, and M. Simonetta, *J. Chem. Soc., Perkin Trans. 2*, 342 (1973).

Scheme I



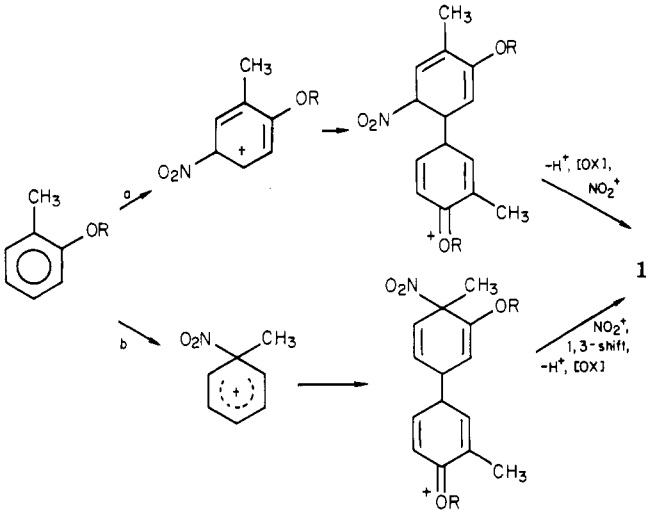
between the C(12) methylene group and the phenyl ring A hydrogen at C(6) are relieved in the normal way for such substituents, viz., through increase in both the C(6)–C-(5)–O(11) and C(5)–O(11)–C(12) angles and concomitant decrease in the C(4)–C(5)–O(11) angle. That this produces some overcrowding of the methyl substituent at C(4) is evident from the 4.6° difference in the exocyclic angles subtended at this center. In addition to these angular deformations, the directly bonded atoms C(1′), N(7), C(10), and O(11) are displaced by 0.017, 0.123, 0.058, and 0.034 Å, respectively, to the same side of the least-squares plane through phenyl ring A atoms.

The dihedral angle between the planes through phenyl ring B carbon atoms and that through C(3′), N(7′), O(8′), and O(9′) is 49.6°. Moreover, owing to the fact that the *C(4′)*-ethoxy substituent is sandwiched between the *C-(3′)*-nitro and *C(5′)*-methyl substituents, C(11′) is forced out of the phenyl ring B plane by 1.111 Å to relieve severe steric overcrowding; the associated C(3′)–C(4′)–O(10′)–C-(11′) torsion angle is −107.1°. As with ring A, additional out-of-plane displacements of directly bonded atoms [C(1), −0.059; N(7′), 0.037; O(10′), −0.108; C(13′), −0.092 Å] contribute to relief of substituent interactions, but there are smaller differences between pairs of exocyclic bond angles at the carbon centers bearing these substituent atoms.

Nitration of 2-(propyloxy)toluene and 2-methylanisole under identical conditions gave similar products (Scheme I).

Formation of biphenyl derivatives in the nitration of aromatic compounds in acetic acid and other solvent systems has been documented previously.[1] Involvement of a cationic intermediate, obtained either by protonation of the aromatic ring[9] or by attack of nitronium ion at the ipso[10] or other position[11] of the ring, has been suggested. The intermediate arising from the ipso attack has been identified by a trapping procedure and other chemical means.[12] Also, a radical cation intermediate has been postulated in the oxidative coupling nitration of alkoxybenzenes.[1] Although the latter type of intermediate has recently been proposed by Perrin to describe the nitration of naphthalene, its involvement has been disputed by others.[13-15] Scheme II indicates two possible ionic mechanism for the present situation.

Scheme II



In the case of alkyl-substituted aromatic compounds, the ipso attack takes place at the carbon bearing the alkyl group. Our attempts to study the suggested intermediate(s) (Scheme II) by NMR at a temperature lower than −35 °C were not successful because the reaction could not be initiated at this temperature, and at the inductive temperature, the reaction proceeds faster than the NMR time scale. In view of the structure of the biphenyl product, a radical cation intermediate seems improbable since such an intermediate would not be expected to couple selectively. Thus, the ionic mechanism (Scheme II), initiated by attack of nitronium ion, favors the present experimental results, although no distinction can be made between the suggested paths.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 180 spectrometer. ^1H NMR spectra were taken with a Varian CFT-20 spectrometer and ^{13}C NMR spectra with a Varian XL-100 instrument. Mass spectra were obtained on a Varian Mat CH5 single-focus medium-resolution spectrometer. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Microanalyses were performed by the staff of Schering's microanalytical laboratory.

Nitration of 2-Ethoxytoluene. The following general procedure was used for the nitration of the 2-alkoxytoluenes covered in this report. To a stirred solution of 70% nitric acid (100 mL) at −10 °C was added 2-ethoxytoluene [bp 127–128 °C (131 mmHg), 12.6 g] at such a rate that the temperature was maintained between −10 and −5 °C. The addition took approximately 90 min, after which the solution was stirred at −10 °C for an additional 2 h. The mixture was then poured on to ice (500 g), neutralized to pH 8 with Na_2CO_3, and extracted with ethyl acetate. The organic extract was treated with Darco (20 g) and dried ($MgSO_4$), and the solvent was removed by rotary evaporation to give a brown oil. TLC (hexane/methylene chloride; 3:7 v/v) indicated three major spots consisting of starting material, mononitrated ethoxytoluene, and a biphenyl derivative; these were followed by several minor and more polar components. This mixture was separated by use of a Waters Pre-500 HPLC instrument, with a silica gel column and a hexane–methylene chloride gradient from 80:20 to 20:80 (v/v).

(8) P. Coggon, A. T. McPhail, and S. C. Wallwork, *J. Chem. Soc. B*, 884 (1970); P. A. Luhan and A. T. McPhail, *J. Chem. Soc., Perkin Trans. 2*, 51 (1973).
(9) I. Puskas and E. K. Fields, *J. Org. Chem.*, **32**, 3924 (1967).
(10) A. Fischer and C. C. Greig, *J. Chem. Soc., Chem. Commun.*, 50 (1974).
(11) I. Puskas and E. K. Fields, *J. Org. Chem.*, **31**, 4204 (1966).
(12) M. W. Galley and R. C. Hahn, *J. Org. Chem.*, **41**, 2006 (1974); A. H. Clemens, M. P. Hartshorn, K. E. Richards, and G. J. Wright, *Aust. J. Chem.*, **30**, 103 (1977); A. Fischer, G. H. Henderson, T. A. Smyth, F. W. B. Einstein, and R. F. Cobbledick, *Can. J. Chem.*, **59**, 584 (1981); K. S. Feldman, A. McDermott, and P. C. Myhre, *J. Am. Chem. Soc.*, **101**, 505 (1978).
(13) C. L. Perrin, *J. Am. Chem. Soc.*, **99**, 5516 (1977).
(14) G. A. Olah, S. C. Narang, and J. A. Olah, *Proc. Natl. Acad. Sci. U.S.A.*, **78**, 3298 (1981).
(15) L. Eberson, L. Johnsson, and F. Rander, *Acta Chem. Scand., Ser. B*, **32**, 749 (1978).
(16) R. W. Miller and A. T. McPhail, *J. Chem. Soc., Perkin Trans. 2*, 1527 (1979).
(17) D. T. Cromer and J. T. Waber, *Acta Crystallogr.*, **18**, 104 (1965).
(18) R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, **42**, 3175 (1965).

The first component, a liquid after removal of solvent, was identical with the starting material.

The second component was identified as 2-ethoxy-5-nitrotoluene: mp 65–66 °C; yield 9.87 g (58%); mol wt 181.19; NMR ($CDCl_3$) δ 8.08 (1 H, dd, J_m = 2 Hz, J_o = 9 Hz), 8.0 (1 H, d, J = 2 Hz), 6.79 (1 H, d, J = 9 Hz), 4.12 (2 H, q, J = 6.5 Hz), 2.26 (3 H, s), 1.47 (3 H, t); IR (Nujol) 1612, 1590, 1520, 1498, 1470, 1458, 1390, 1378, 1260, 1142, 1118, 1100, 1040, 940, 902, 812, 780, 750, 718, 658 cm^{-1}. Anal. Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.12; H, 6.04; N, 7.48.

The third component was identified as 2,3′-dinitro-4,5′-dimethyl-5,4′-diethoxybiphenyl: mp 158–159 °C; yield 1.4 g (4.2%); mol wt 360.37; NMR ($CDCl_3$) δ 7.82 (1 H, brs), 7.54 (1 H, d, J = 2.5 Hz), 7.21 (1 H, d), 6.59 (1 H, brs), 4.10 (4 H, 2 q, J = 7 Hz), 2.35 (3 H, s), 2.28 (3 H, s), 1.48 (6 H, 2 t); IR (Nujol) 1618, 1562, 1540, 1520, 1470, 1380, 1362, 1342, 1300, 1280, 1262, 1242, 1230, 1195, 1180, 1118, 1050, 1035, 1005, 940, 920, 912, 902, 888, 830, 810, 795, 775, 750, 725, 662 cm^{-1}. Anal. Calcd for $C_{18}H_{20}N_2O_6$: C, 59.99; H, 5.59; N, 7.77. Found: C, 60.19; H, 5.27; N, 7.54.

Nitration of 2-Methylanisole. 2-Methylanisole [bp 119 °C (143 mmHg), 12.2 g] was nitrated as described above.

2-Methyl-4-nitroanisole: mp 50–51 °C; yield 4.9 g (29%); mol wt 167.17; NMR ($CDCl_3$) δ 8.10 (1 H, dd, J_m = 2.5 Hz, J_o = 9 Hz), 8.02 (1 H, d, J_m = 2.5 Hz), 6.81 (1 H, d), 3.92 (3 H, s), 2.26 (3 H, s); IR (Nujol) 1610, 1592, 1510, 1498, 1460, 1440, 1380, 1340, 1260, 1186, 1148, 1100, 1042, 1020, 995, 930, 898, 828, 810, 755, 715, 640 cm^{-1}. Anal. Calcd for $C_8H_9NO_3$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.49; H, 5.60; N, 8.41.

2,3′-Dinitro-4,5′-dimethyl-5,4′-dimethoxybiphenyl: mp 168–169 °C; yield 0.75 g (2.3%); mol wt 332.32; NMR ($CDCl_3$) δ 7.74 (1 H, brs), 7.59 (1 H, d, J = 2 Hz), 7.27 (1 H, d), 6.65 (1 H, brs), 3.94 (3 H, s), 3.92 (3 H, s), 2.38 (3 H, s), 2.28 (3 H, s); IR (Nujol) 1620, 1570, 1530, 1505, 1460, 1380, 1360, 1340, 1298, 1260, 1240, 1180, 1115, 1045, 1002, 902, 890, 870, 820, 780, 760, 740 cm^{-1}. Anal. Calcd for $C_{16}H_{16}N_2O_6$: C, 57.83; H, 4.85; N, 8.43. Found: C, 57.82; H, 4.69; N, 8.46.

Nitration of 2-(Propyloxy)toluene. 2-(Propyloxy)toluene [bp 135–137 °C (130 mmHg), 15 g] was nitrated as described above.

2-(Propyloxy)-5-nitrotoluene: liquid; yield 10.94 g (56%); mol wt 195.22; NMR ($CDCl_3$) δ 8.03 (1 H, dd, J_m = 2.5 Hz, J_o = 9 Hz), 7.86 (1 H, d, J = 2.5 Hz), 6.73 (1 H, d), 3.96 (2 H, t, J = 6 Hz), 2.33 (3 H, s), 1.8 (2 H, m), 1.06 (3 H, t); IR (Nujol) 1610, 1588, 1520, 1498, 1472, 1460, 1392, 1380, 1260, 1145, 1118, 1100, 1050, 940, 900, 812, 782, 755, 718, 660 cm^{-1}. Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.53, H, 6.71, N, 7.17. Found: C, 61.56; H, 6.44; N, 7.22.

2,3′-Dinitro-4,5′-dimethyl-5,4′-bis(propyloxy)biphenyl: mp 141–142 °C; yield 2.75 g (7%); mol wt 388.42; NMR ($CDCl_3$) δ 7.89 (1 H, brs), 7.57 (1 H, d, J = 2 Hz), 7.27 (1 H, d), 6.64 (1 H, brs), 3.97 (4 H, 2 t, J = 6 Hz), 2.36 (3 H, s), 2.31 (3 H, s), 1.83 (4 H, m), 1.08 (6 H, 2 t); IR (Nujol) 1615, 1560, 1538, 1520, 1500, 1460, 1380, 1318, 1300, 1260, 1230, 1180, 1158, 1110, 1080, 1030, 998, 960, 910, 870, 800, 778, 760, 740, 720, 660 cm^{-1}. Anal. Calcd for $C_{20}H_{24}N_2O_6$: C, 61.85; H, 6.23; N, 7.21. Found: C, 62.17; H, 6.30; N, 7.53.

Crystal data: $C_{18}H_{20}N_2O_6$(I), mol wt 360.37; monoclinic; a = 7.878 (3) Å, b = 8.204 (3) Å, c = 27.843 (11) Å, β = 91.36 (3) Å, U = 1799 Å^3, Z = 4, d_{calcd} = 1.331 g cm^{-3}; absorption coefficient for Cu Kα radiation (λ = 1.5418 Å), μ = 8.6 cm^{-1}. Space group $P2_1/c(C^5_{2h})$ was uniquely established from the systematic absences $0k0$ when $k \neq 2n$ and $h0l$ when $l \neq 2n$.

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Registry No. 1, 82280-90-8; 2-ethoxytoluene, 614-71-1; 2-methylanisole, 578-58-5; 2-propyloxytoluene, 4607-37-8; 2-ethoxy-5-nitrotoluene, 70611-03-9; 2-methyl-4-nitroanisole, 50741-92-9; 2,3′-dinitro-4,5′-dimethyl-5,4′-dimethoxybiphenyl, 82280-91-9; 2-(propyloxy)-5-nitrotoluene, 82280-92-0; 2,3′-dinitro-4,5′-dimethyl-5,4′-bis(propyloxy)biphenyl, 82280-93-1.

Supplementary Material Available: Crystallographic measurements, interatomic distances and angles (Figure 2), monohydrogen atom fractional coordinates (Table II), tables of least-squares plane equation data (Table III), torsion angles (Table IV), anisotropic thermal parameters (Table V), calculated hydrogen atom fractional coordinates (Table VI), and observed and calculated structure amplitudes (Table VII) (16 pages). Ordering information is given on any current masthead page.

Free Radicals in Synthesis. 1. A Two-Step Carbolactonization Procedure

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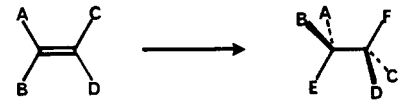
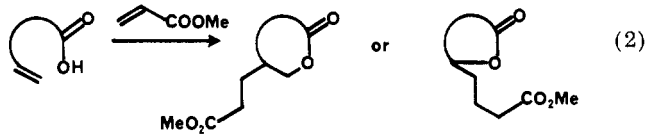
The vicinal functionalization of unactivated olefins with regio- and stereochemical control (generalized in eq 1) is



(1)

an important area of development in organic synthesis.[1] In connection with an ongoing synthetic program, we have made an initial foray into this area, the results of which are described herein.

We required a reliable means of carbolactonization (eq 2) whereby the olefinic linkage became vicinally func-



(2)

tionalized by carboxylate and acrylate residues, respectively. A direct formation of the new carbon–oxygen and carbon–carbon bonds in a single step would be ideal. Unfortunately, the acrylate unit is not a suitable electrophilic trigger for the direct carbolactonization sought. However, the well-established mercurio-,[2] iodo-,[3] and selenolactonization[4] reactions and the demonstrated reductive cleavages of the respective C–Hg,[5] C–I,[6] and C–Se[7] bonds by borohydride salts or hydridostannanes held the promise of an acceptable solution. We therefore executed a systematic study of lactones **1a–c**, **2a–c**, and **3a–c** to compare the acetoxymercurio, iodo, and phenylseleno substituents as functional auxiliaries for the generation of

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